30. The isolated raffinose synthase gene of claim 1, wherein the hybridization temperature is 65°C to 68°C.--

REMARKS

The Office Action of May 2, 2000 presents the examination of claims 1-10 and 16-23. Claims 1-10, 16, 21 and 22 are amended. Claims 28-30 are added for consideration of the Examiner. Support for claims 28 and 29 is found in the specification, such as on page 29, lines 16-24, to page 30, lines 1-12. Support for claim 30 is found on page 18, lines 12-13, of the specification. No new matter is inserted into the application.

Rejection Under 35 U.S.C. § 101

The Examiner rejects claims 1-10 and 16 under 35 U.S.C. § 101 for allegedly being directed toward non-statutory subject matter. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are requested.

The Examiner views the claims as reading upon a gene in its naturally occurring form. In response to the Examiner's remarks, Applicants amend claims 1-10 and 16 to read "An isolated raffinose synthase gene" or "An isolated nucleic acid", as suggested by the Examiner. Thus, the instant rejection is overcome.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1 and 16-23 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly not being enabled by the specification. This rejection is respectfully traversed. Reconsideration of the claims and withdrawal of the instant rejection are requested.

The Examiner appears to include arguments directed to written description in addition to arguments regarding enablement. Thus, Applicants address each of these below.

The present invention provides novel raffinose synthase genes from various species of plants and methods for introducing them into host cells and using them to produce raffinose synthase. The Examiner concludes that the specification does not

teach one skilled in the art how to generically produce transformants expressing raffinose synthase activity.

Enablement

Claims 1 and 16-23 are specifically rejected because the specification allegedly does not enable the "isolation of other nucleotide sequences which are hybridizable to a nucleotide sequence claimed in claim 1". The Examiner indicates that the specification does not enable a person skilled in the relevant art to make and/or use the invention in a way that is commensurate with the scope of these claims. Applicants respectfully disagree.

The factors to be considered in determining enablement are set forth in *In re Wands*, 8 USPQ2d 1400. The amount of experimentation is not determinative, rather the issue is whether such necessary experimentation is undue. Furthermore, experimentation that is expected to have to be conducted by the skilled artisan is not considered undue.

Among the factors to be considered are the nature of the invention, the scope of the claims, and the level of ordinary skill in the art. The present invention is cloned nucleic

acids, vectors, host cells, and methods for using each. The level of skill in the art of molecular biology is taken to be high. The claims include limitations that the nucleic acids hybridize to enumerated sequences and encode amino acid sequences that provide an enzyme having a defined activity.

A critical factor is the amount and guidance provided by the specification to the practitioner, including the presence or absence of working examples. In this regard, the Examiner is referred to the following disclosures in the specification, which provide description and guidance for one skilled in the relevant art to isolate other nucleotide sequences that are hybridizable to a nucleotide sequence as described in claim 1:

1. The detailed description provides on page 8 lines 7-10 that the raffinose synthase genes can be isolated from soybean, and plants belonging to the families *Chenopdiaceae* (such as the beet) and *Cruciferae* (mustard, rapeseed).

2. Examples of isolated raffinose genes and protein encoding sequences are provided in SEQ ID NO: 1-8; these are examples of nucleotide sequences that can be successfully isolated following the teachings of the present specification. The techniques presented in the specification may be utilized by

those skilled in the relevant art to screen other organisms' genomes for a raffinose synthase gene.

3. The raffinose gene sequence can be isolated from other plants as by the isolation from soybean, as described in the specification at page 9, lines 17-25 and page 10, lines 1-17. Specifically, this description provides for the isolation of a sequence in claim 1 starting from plant tissue. The methods described therein include RNA extraction from a frozen tissue sample using a standard RNA extraction kit, subsequent ethanol precipitation, and fractionation of the poly-A tail using standard methods, followed by cDNA synthesis using a standard cDNA synthesis kit. DNA amplification instructions are described using the sequence in SEQ ID NO: 2 and using the templates and primers designed by standard molecular biology techniques. This raffinose synthase gene isolation process is repeated for a *Chenopdiaceae* plant on page 11 lines 14-25 and page 12 lines 1-20; and for a *Cruciferae* plant on page 13 lines 20-25 and page 14 lines 1-25, and page 15 lines 1-6.

Another important factor is the state of the art at the time the invention was made. The Examiner takes a position that the skilled artisan would not know *a priori* what portions of a

raffinose synthase gene are necessary to encode a polypeptide having the desired activity. Applicants point out that synthesis of libraries of large numbers of mutants, particularly once a cloned gene is in hand, and their screening, is a standard practice in the art, and as such, is not undue experimentation. In this regard, the specification describes an assay for raffinose synthase activity that can be applied to candidate clones. The Examiner is directed to page 31, lines 21-25 of the specification.

The Examiner seems to be relying upon an assertion that the art of heterologous gene expression is inherently unpredictable. However, the issue here is not, as the Examiner asserts, whether the practitioner of the invention can predict beforehand what nucleic acid sequence must be produced to obtain a functional raffinose synthase. Rather, the issue is whether the practitioner can predict that, following the teachings of the specification, a nucleic acid sequence that hybridizes to one or more of the sequences enumerated in claim 1 and encodes a functional raffinose synthase can be isolated. Applicants submit that it is very predictable that a nucleic acid encoding a functional raffinose synthase can be isolated from a library

of mutants starting from one of the enumerated sequences or from a library of plant nucleic acids.

For all of the above reasons, the present specification should be considered enabling of the presently claimed invention.

Lack of Written Description

In arguments against enablement, the Examiner introduces arguments that appear to assert a rejection based on a lack of written description of nucleic acid variants not explicitly disclosed in the specification or claims. The Examiner correctly argues that adequate written description requires an indication of a structural OR functional characteristic of the compounds the applicant wishes to claim. However, the Examiner overlooks that Applicants have recited common functional characteristics to sufficiently define the generic subject matter.

Specifically, the specification indicates that the nucleic acids of the invention i) hybridize with a nucleotide sequence recited in claim 1, and ii) encode a polypeptide having the enzymatic activity recited in claim 1. Applicant has provided

several examples of sequences that have been isolated, hybridized, and demonstrated sufficient activity using the method described in the specification. Thus the disclosure of the specification is sufficient to meet the written description requirement as set forth in *Univ. of California v. Eli Lilly v. Univ. of California*, 43 USPQ2d 1398 (Fed. Cir. 1997). Accordingly, the Examiner's arguments grounded in lack of written description are rebutted.

The experimentation required to determine if any particular embodiment of the claimed invention provides active raffinose synthase does not amount to undue experimentation. The specification provides disclosure of a process for obtaining the genetic sequence encoding the raffinose synthase gene of any organism based on the description of the process of cDNA isolation from soybean, mustard seed, beet, or rapeseed. The specification adequately discloses a number of species of the invention and describes a common functional feature they all share.

Thus, the specification provides adequate written description and enablement of the claimed invention. Thus, the

rejection of claims 10, and 16-23 under 35 U.S.C. § 112 first paragraph, should be withdrawn.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1 and 16-23 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are requested.

In particular the Examiner objects to usage of "hybridizable" and "stringent conditions" as unclear whether the stringency of the condition is low, medium or high. In response to the Examiner's remarks, Applicants amend claim 1 to incorporate hybridization conditions. The recited hybridization conditions are present in the specification at page 18, lines 11-13.

Applicants point out that claim 16 is an independent claim that the Examiner erroneously pointed out as a dependent claim. Also, the "hybridizable" and "stringent conditions" language that the Examiner objects to is not present in independent claim 16 or dependent claims 17-23. Therefore the objection to claim 1 above should not apply to claims 16-23.

Claims 1-10 and 16-23 are considered vague due to the language "represented by." In response to the Examiner's remarks, Applicants amend the claims to delete "represented by" and insert "as depicted by", as suggested of the Examiner.

Finally, claims 16, 19-20 are rejected for allegedly being vague for the recitation of "nucleic acid exhibiting promoter activity in a host cell". Specifically, the Examiner states that it is unclear if the Applicants intended nucleic acid molecules such as introns, promoters, enhancers, transcription factors, and subgenomic sequences to be included in this definition. Applicants submit that the amendment of the claims to recite "promoter" adequately defines the invention.

Applicants submit that the above amendments to the claims fully address each ground of rejection under 35 U.S.C. § 112, second paragraph. Thus, the instant rejection is overcome.

Rejection under 35 U.S.C. § 102(b)

Claims 1-10, 16, 18-19, and 22 are rejected under § 102(b) for allegedly being anticipated by Castillo et al. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are requested.

The present invention is not anticipated by Castillo et al. because the reference discloses only the presence of active raffinose synthase in developing soybean seed and a partial purification of the protein. Disclosure of the presence of active raffinose synthase in a plant is not disclosure of an isolated nucleic acid encoding a raffinose synthase. Applicants note that the Examiner was interpreting the previous claim to include a raffinose synthase gene within a plant in nature. Applicants have amended the present claims to recite "an isolated" nucleic acid or gene to provide for patentable subject matter. Castillo does not teach the isolation of any gene coding for a raffinose synthase protein or even the complete isolation of a raffinose synthase protein, which might be used to obtain sequence data for designing a probe for a cloning experiment. Thus, Castillo is not enabling of the present invention and as such cannot anticipate it.

For all the above reasons, the invention of claims 1-10, 16, 18-19, and 22 is not anticipated by Castillo et al. Accordingly, the present rejection of these claims under 35 U.S.C. § 102 (b) over the cited claims should be withdrawn.

Obvious-Type Double Patenting

The Examiner provisionally rejects claims 1-10, 16-23 under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1-4, 6-18, 30-36, 40-41, 43-44 of copending Application No. 08/992,914.

In response to this rejection, Applicant's representative submits the terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) attached hereto. Thus, the instant rejection is overcome.

If there are any minor matters precluding allowance of the application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. (Reg. No. 36,623) at (703) 205-8000.

Pursuant to the provisions of 37 C.F.R. § 1.17 and 1.136(a), Applicants hereby petition for an extension of three (3) months for the period in which to file a response to the outstanding Office Action. The required fee of $890.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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